Applicants: Cornelia J. Forster et al.
Application No.: 10/632,340

REMARKS

The Claim Amendments

Applicants have canceled claims 16-17 and 19-22. Applicants have amended claim 18 to recite a method of treating diabetes, anxiety, schizophrenia, bipolar disorder, depression or stroke with a composition of the invention. Applicants have amended claim 23 to correct its dependency and to recite the use of an additional therapeutic agent selected from an antipsychotic agent, an agent for treating stroke, an antidepressant, or an agent for treating diabetes. Support for these amendments may be found in the originally-filed claims and throughout the specification.

None of these amendments adds new matter. Their entry is requested.

Applicant reserves the right to pursue canceled subject matter in this application or in future continuing or divisional applications.

The Response

The Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 16-17 and 19-20 under 35 U.S.C. §112, first paragraph. The Examiner states that the specification, while being enabling for a method of treating leukemia, does not reasonably provide enablement for a method of treating any or all diseases or conditions. The Examiner further states that the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses recited in the claims. The Examiner also asserts that diseases such as bipolar disorder are "very difficult to treat and at present there is no known drug [that] can successfully lessen the course of [this disease]".

Applicant respectfully disagrees with the Examiner's rejection, but has canceled claims 16 and 17 and amended claim 18 to expedite prosecution. Amended claim 18 recites a method of treating diabetes, schizophrenia, anxiety, bipolar disorder, depression or stroke with a composition of the invention, while amended claim 23 recites the additional step of administering an additional therapeutic agent

selected from an antipsychotic agent, an agent for treating stroke, an antidepressant, or an agent for treating diabetes.

These claims are clearly enabled by the specification. In particular, the specification teaches methods of administering GSK-3 inhibitors of the invention (see, e.g., [0064] to [0075] on pages 17-19). The specification also discloses that the GSK-3 inhibitors of the invention may be used to treat diabetes, anxiety, depression, stroke, schizophrenia or bipolar disorder (see, e.g., [0088] to [0091] on page 22). Further, the specification teaches various additional therapeutic agents that can be used to treat diabetes, depression, stroke, schizophrenia or bipolar disorder (see, e.g., [0077] to [0079] on page 20). Thus, the specification as originally filed fully enables the claimed invention.

Further, the use of GSK-3 inhibitors to treat the claimed diseases was well established at the time the invention was made in *in vivo* animal models. With respect to stroke, the specification exemplifies a rat model of stroke (the Middle Cerebral Artery Occlusion Model (MCAO)) and shows that treatment with a compound of formula I "was able to significantly reduce striatal ischemic damage" and reduce edema formation in this model of stroke. In addition, rats treated with a compound of the invention "demonstrated marked improvement in neurological function over the time course of the experiment." See, e.g., Example 19 on pages 34-38 and Figures 1 and 2.

The specification exemplifies a rat model of depression and demonstrates that compounds of the invention showed anti-depressant activity in the model. See, e.g., Example 20 on pages 38-39. Similarly, the specification exemplifies mouse models of schizophrenia and anxiety and shows that compounds of the invention have anti-schizophrenic and anxiolytic effects in the respective animal models. See, e.g., Examples 21 and 22 on pages 39-42. Further, the specification teaches that lithium, a agent that has been used for decades to treat bipolar disorder, acts by decreasing GSK3 activity (see, e.g., [0012] on page 4). Taken together with the animal models that compounds of the invention are useful in treating psychiatric disorders, one

skilled in the art would reasonably expect that a GSK3 inhibitor of the invention could be used to treat bipolar disorder successfully.

With respect to diabetes, Cline et al., *Diabetes* 51: 2903-2910, 2002 (hereafter "Cline") disclosed that a GSK-3 inhibitor treatment activated glycogen synthase activity in the Zucker diabetic fatty (ZDF) rat model of diabetes, which significantly improved oral glucose disposal and significantly lowered fasting plasma glucose in diabetic rats (see, e.g., page 2909, right column). Similarly, Henriksen et al., *J. Physiol. Endocrinol. Metab.* 284: E892-E900, 2003 (hereafter "Henriksen") showed that administration of a GSK-3 inhibitor to insulin-resistant diabetic ZDF rats improved whole body glucose disposal and insulin sensitivity (see, e.g., page E899, right column). Taken together with the specification, Cline and Henriksen clearly show that there is a reasonable correlation between the GSK-3 inhibitors of the invention, the *in vitro* data showing their GSK-3 inhibitory activity, and the use of these compounds to treat diabetes. Cline and Henriksen are enclosed in a Supplemental Information Disclosure Statement filed concurrently herewith.

For the above reasons, the specification and prior art demonstrate that GSK-3 inhibitors are efficacious in animal models that are predictive of the claimed diseases or conditions in humans. Thus, the claimed methods are fully enabled by the specification.

The Obviousness-Type Double Patenting Rejection

The Examiner has rejected claims 1-23 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-15 of United States Patent 6,696,452 (hereafter "the '452 patent").

Applicants stand ready to provide a terminal disclaimer over the '452 patent upon indication of allowable subject matter.

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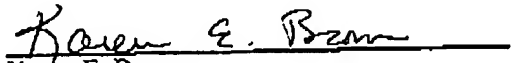
Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,



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